DEPARTMENT OF HEALTH AND HUMAN SERVICE

Southwest Region

Food and Drug Administration
Denver District Office
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October 12, 2000

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Richard Hollowell, President/C.E.O.
Kanox, Inc.
1200 North Grande, P.O. Box 3007
Hutchinson, Kansas 67501

Ref. #: DEN-01-2

Dear Mr. Hollowell:

During an inspection of your firm, Kanox Inc., 1405 South Platte River Drive, Denver, CO on August 30 – September 8, 2000, Consumer Safety Officers Daniel J. Lahar, and Karen G. Hirshfield determined that your firm manufacturers and distributes Oxygen USP. Oxygen USP is a drug product as defined by section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection revealed that your product, Oxygen USP, is adulterated under Section 502(a)(2)(B) of the Act in that the controls used for the manufacturing, processing, packing, or holding of this product are not in conformance with current Good Manufacturing Practice Regulations (GMPs) [Title 21, Code of Federal Regulations (21 CFR), parts 210 and 211].

Deviations noted during the inspection include, but are not limited to the following:

1. Failure to assay the incoming liquid Oxygen USP for identity and strength prior to release [21 CFR 211.165(a)]. Specifically, liquid Oxygen USP lot number 0670KCA00021D, consisting of (XXXXX) received on or around (XX), did not undergo identity and purity testing prior to distribution of at least (X) lots.

2. Failure to properly calibrate the Oxygen Analyzer used for the assay of Oxygen, USP, [21 CFR 211.160(b)(4)]. For example, 1) the firm's calibration log for the Oxygen Analyzer shows that the analyzer was not calibrated prior to (XXX) However, the analyzer was used to test and release at least (X) lots that were manufactured and distributed prior to this date; 2) the manufacturer requires the analyzer to be re-calibrated

if more than a 10°C change has occurred from the previous calibration. Your analyzer is positioned next to the dock doors and is exposed to outdoor temperature fluctuations. However, according to the firm's employee responsible for calibration, re-calibration is not always done when such a temperature fluctuation occurs; or if it is done, it is not documented; 3) the analyzer manufacturer requires a weekly filter check, but this check is not being documented.

3. Failure to establish and maintain written procedures for all production and process controls [21 CFR 211.100(a)]. For example, there are no written procedures for: the identity and strength specifications for incoming liquid Oxygen USP, the calibration frequency for the Oxygen Analyzer, defining the quarantine areas within the warehouse, and defining what is an adverse drug event that would require FDA notification. In addition, there is no documentation to show that the written procedures are drafted, reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality control unit.

4. Failure of the laboratory records to contain the initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards [21 CFR 211.194(a)(8)]. For example, entries on the Servomex Calibration Log for 6/1/00 and 6/2/00 not only show that one person performed and reviewed the same work, but it also shows that the review was done before the testing was conducted (i.e., the date of review was 5-30-00).

At the conclusion of this inspection, Consumer Safety Officers Lahar and Hirshfield issued a written report of Inspectional Observations (FDA-483) to Branch Manager James R. Hill. A copy of the FDA-483 is enclosed for your reference.

We acknowledge your written response (undated, but postmarked October 5, 2000) to the inspectional observations presented to Mr. Hill at the close of the inspection. The corrections described appear to correct the deficiencies involving observations 2, 3, 4, 6, 7, 8 and 9 of the FDA-483. The letter has been added to your company file, and the corrections will be verified at the next inspection.

Observation number one involved the failure to establish that the test procedure used to determine the strength and identity of Oxygen, USP, will provide test results that are equivalent or superior to those obtained using the official test procedure [21 CFR 211.165(e)]. The Operator's Manual available during the inspection showed that the Oxygen Analyzer, Servomex (XXXXX), has an accuracy range of +/- 1.0 percent of span, which is not equivalent to the USP method, which has an accuracy of +/- 0.1%. Your firm provided to our Investigators the June 28, 2000 memorandum from the Oxygen Analyzer manufacturer (Servomex). The manufacturer's memorandum states that new validation work has been conducted to show USP equivalence. However, the documentation to support equivalency, such as the actual validation test results or an updated operator's manual showing the corrected accuracy claim, were not available by the close of the inspection and were not provided in your written response. Please provide these records in your written response to this letter.

The timeframes given for the corrective action for Observation 5 (XXXXXX) and 10 (no date given) also appear to be too long. Please explain the delay in implementing these corrective actions.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. As C.E.O., it is your responsibility to assure adherence with all requirements of the Act and current GMP Regulations.

These deviations may be indicative of corporate wide non-compliance. Internal audits should be conducted at all your medical gas facilities and appropriate action be taken to assure that similar violations are not occurring at other locations. This letter serves as official notification that FDA expects all locations to be in compliance. Guidance documents explaining the requirements for compressed medical gases can be found at our Internet website http://www.fda.gov/cder/dmpq/cgmpnotes.htm.

By copy of this letter, we are advising the Health Care Financing Administration (HCFA) that our inspection of your firm revealed significant deviations from the Food, Drug and Cosmetic Act. They may elect to defer or discontinue payment for any health care product in violation of state or federal law.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action, including seizure or injunction, without further notice. Federal agencies are advised of the issuance of all warning letters so that they may take this information into account when considering the award of contracts.

Please advise this office in writing, within fifteen (15) working days after receipt of this letter, of any additional actions you have taken to correct the violations. Your response should include:

(1) each step that has or will be taken to completely correct the current violations and prevent the recurrence of similar violations;
(2) the time when correction will be completed;
(3) any reason why the corrective action is not completed within the response time;
(4) any documentation necessary to indicate correction has been achieved

Your response should be sent to the attention of Ms. Regina A. Barrell, Acting Compliance Branch Director, at the above letterhead address.

Sincerely,

Thomas A. Allison
District Director

Enclosure: FDA-483